

## PS 14

## Non-genetic determinants of type 2 diabetes

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## Effect of alpha-tocopherol and beta-carotene supplementation on the incidence of type 2 diabetes in Finnish male smokers

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**Background and Aims:** Type 2 diabetes is associated with reduced antioxidant defenses. Only a few studies in humans have emerged about the preventive effect of antioxidants on diabetes. The aim of this study was to determine whether alpha-tocopherol and beta-carotene supplementation would reduce the incidence of type 2 diabetes in Finnish male smokers.

**Materials and Methods:** The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study, a randomized, double-blind, placebo-controlled trial with 2x2 factorial design, randomized 29 133 male smokers aged 50–69 years to receive either vitamin E: 50 mg/d, or beta-carotene 20 mg/d, or both, or placebo for a median of 6. years. During the follow-up (intervention plus 4.5 years postintervention) 1187 incident cases of diabetes were observed among the 27 861 men not reporting diabetes at baseline. The main outcome was drug-treated diabetes identified from a nationwide registry of patients receiving drug reimbursement.

**Results:** The relative risk for diabetes between alpha-tocopherol recipients and non-recipients was reduced (RR 0.87 95%CI, 0.77–0.98) when excluding first two follow-up years. In participants with no clinical abnormalities for metabolic syndrome, the preventive effect of supplemental alpha-tocopherol was stronger (RR 0.64 95%CI, 0.41–0.98). Supplemental beta-carotene had no effect on diabetes.

**Conclusion:** Since type 2 diabetes is an increasing health problem with many severe complications even a small preventive effect of alpha-tocopherol could have notable public health impact. However, more conclusive studies are needed before specific measures to increase the intake of vitamin E are justified. In the meantime it is prudent to consume a lot of vegetables and fruits, foods associated with a healthy life.

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## Association of pulse pressure with fasting hyperglycemia in the general population

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**Background and Aims:** Hypertension is an established key component of metabolic syndrome (MS) associated to obesity, in particular visceral obesity. Pulse pressure (PP), a measure of arterial stiffness, is associated to obesity, hypertension, and diabetes. Aims of this study is to evaluate the prevalence of PP in the diagnosis of MS, its association with the MS impairments, and the categories of glucose tolerance.

**Materials and Methods:** A cohort of inhabitants of Florence, Italy, participating to a screening study for diabetes. 3112 (1748 F, 1364 M) subjects, with no history of diabetes, aged (mean±SD) 55.2±11.5 yrs, with a BMI 26.0±4.2 kg/m<sup>2</sup>, waist circumference 84.3±11.4 cm in F, and 97.6±10.3 cm in M were studied. After overnight fasting (>8 hrs) blood samples for glycemia, total and HDL cholesterol, triglyceride were collected; those subjects with a fasting plasma glucose (FPG) <126 mg/dl underwent a standard OGTT (75 g); anthropometric and clinical parameters as systolic, diastolic, PP, and mean blood pressure (MBP) were measured. MS was defined according to National Cholesterol Education Program (NCEP) criteria.

**Results:** 2134 (75%) subjects presented normal glucose tolerance, 272 (8.7%) impaired glucose tolerance (IGT), 186 (6.0%) impaired fasting glucose (IFG), and 209 (6.7%) were affected by diabetes mellitus (DM). According to NCEP criteria 541 (17.4%) individuals showed fasting plasma glucose ≥110 mg/dl, 1178 (37.8%) hypertension, 957 (30.7%) pathological waist circumference (waist >88 cm in F and >102 cm in M), 416 (13.4%) low HDL cholesterol, and 631 (20.3%) hypertriglyceridemia; 492 (15.8%) of

subjects resulted affected by MS. PP values resulted 45.8±13.0 mmHg, and MBP values 109.1±14.0 mmHg. Subdividing PP and MBP in quintiles, it was observed a progressive increase of prevalence of each MS impairment from the 1<sup>st</sup> to 5<sup>th</sup> quintile. In particular, prevalence of diabetes was 7 fold increased from the 1<sup>st</sup> to 5<sup>th</sup> quintile of PP versus 2 fold and 3 fold increase of prevalence of IGT, and IFG, respectively. At multivariate analysis, PP was significantly (p<0.01) associated with FPG even after adjustment for sex, age, BMI, and mean blood pressure.

**Conclusion:** Elevated pulse pressure is associated with components of the metabolic syndrome, and with fasting hyperglycaemia in particular, independent of high mean blood pressure, age, and adiposity.

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## The correlation between reactions to the stress and the age of onset of type 2 diabetes

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**Background and Aims:** Stress is considered as one of the factors related to the development of Type 2 diabetes. However, severity of reactions to the stress may be various between individuals. The aim of the study was to clarify whether the severity of reactions to the stress affects to development (earlier disease manifestation) of Type 2 diabetes.

**Materials and Methods:** Sixty seven Type 2 diabetic patients (18 males; mean age 61.4±7.4 years; mean diabetes duration 9.8±13.4 years; mean HbA1c level 8.3±1.9%) reported about severity of the reaction to 10 typical stressful life events (SLE) during their adult life before the onset of diabetes: death of a husband/wife, divorce, separation from husband/wife, imprisonment, death of a relative, serious illness, marriage, dismissal, reconciliation with a husband/wife, retirement. To evaluate the stress severity visual analog scale (VAS; 0–10 score) was applied. The patients were divided into two groups according the ratio: summarized VAS score/total number of SLE. Group 1 consists of patients with high ratio (> mean value) or with "severe" reaction to the stress. Group 2 consists of ones with low ratio (< = mean value) or with "mild" reaction to the stress. The age of the diabetes onset was compared.

**Results:** Mean number of SLE for all patients was 4.3±1.7; mean summarized VAS score - 36.2±17.7; mean VAS/SLE ratio value 8.4±4.1. Mean age of the onset of Type 2 diabetes in patients of group 1 ("severe" reaction to the stress, n=32) was younger than in patients of group 2 ("mild" reaction to the stress, n=35): 49.5±9.5 vs 54.2±9.0 (Mann-Whitney U test p=0.05). Besides that the number of patients with the onset of coronary heart disease (CHD) before 55 years old in group 1 was significantly higher (5 vs 0; p<0.02).

**Conclusion:** These data demonstrate that "severe" reaction to the SLE is associated with earlier onset of Type 2 diabetes. The individuals who react to stress more intensive probably represent the group of high risk of early Type 2 diabetes manifestation. The problem needs follow investigation with relation to both Type 2 diabetes and cardiovascular diseases.

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## Occupational stress and low emotional support increase synergistically the risk for future type 2 diabetes in middle-aged women

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**Background and aims:** Psychosocial stress and depressive symptoms are shown to be risk factors for development of type 2 diabetes. The biological mechanisms explaining this diabetogenic effect include behavioural aspects such as obesity, physical inactivity, smoking and unhealthy drinking and also neuroendocrine pathways, with activation of the hypothalamus-pituitary-adrenal (HPA) axis and increased levels of stress hormones, leading to visceral obesity and insulin resistance. However, the origin of the psychosocial stressors, that are players on these biological systems, are not as well described. Our aim was to investigate the association between psychosocial conditions and life style and future development of type 2 diabetes in middle-aged men and women.

**Material and methods:** A prospective case-referent study nested within an ongoing population based health survey in primary care in northern Sweden. All participants in the health survey (n=33,336) in the city of Umeå with surrounding municipalities (135 000 inhabitants) were included. 137 cases, initially non-diabetic but diagnosed with type 2 diabetes after 5.4±2.6 years, were identified and two age- and sex-matched referents, non-diabetic after 8.1±2.5 years, for each case. Occupational stress,